# AMENDMENTS TO THE CLAIMS

Claims 21-22 (cancelled).

23. (currently amended): The pharmaceutical composition according to claim 21 wherein said peptide analogue has the A pharmaceutical composition for the gastrointestinal delivery by oral administration of an LH-RH peptide analogue, said composition comprising a therapeutically effective amount of a peptide analogue in combination with  $\alpha$ -cyclodextrin and excipients suitable for the gastrointestinal delivery of the peptide analogue, wherein the  $\alpha$ -cyclodextrin enhances the biological activity of of the LH-RH peptide analogue when orally administered, said LH-RH peptide analogue having the formula (SEQ ID N°: 1):

A1-A2-A3-A4-A5-A6-A7-A8-Pro-Z (A)

- Al is pGlu; D-pGlu; Sar; AcSar; Pro or a derivative thereof; Ser; D-Ser; Ac-D-Ser; Thr; D-Thr; Ac-D-Thr; or an aromatic D-amino acid which may be acylated;
- A2 is a direct bond; His; or an aromatic D-amino acid;
- A3 is an aromatic L- or D-amino acid;
- A4 is Ala, Ser, D-Ser, MeSer, Ser(OBut), Ser(OBzl) or Thr;
- A5 is an aromatic L-amino acid; or a basic L- or D-amino acid;
- A6 is Gly; (S)-spirolactam-Pro; D-Pro; D-Ser; D-Thr; D-Cys; D-Met; D-Pen; D-(S-Me)Pen; D-(S-Et)Pen; D-Ser(OBu<sup>t</sup>); D-Asp(OBu<sup>t</sup>); D-Glu(OBu<sup>t</sup>); D-Thr(OBu<sup>t</sup>); D-Cys(OBu<sup>t</sup>); D-Ser(OR<sub>1</sub>) where R<sub>1</sub> is a sugar moiety; an aza-amino acid; D-His which may be substituted on the imidazole ring by a (C<sub>1</sub>-C<sub>6</sub>)alkyl, a (C<sub>2</sub>-C<sub>7</sub>)acyl or a benzyl group; an aliphatic D-amino acid with a (C<sub>1</sub>-C<sub>8</sub>)alkyl or a (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl side

chain ; an aromatic D-amino acid ; D-cyclohexadienyl-Gly ; Dperhydronaphthyl-Ala; D-perhydrodiphenyl-Ala; or a basic Lor D-amino acid;

- A7 is a linear, branched or cyclic aliphatic L-amino acid of 3 to 20 carbon atoms which may be N-alpha-substituted by a  $(C_1-C_4)$  alkyl group optionally substituted by one or several fluorine atoms;
- A8 is a basic L- or D-amino acid;
- Z is  $GlyNH_2$ ; D-AlaNH $_2$ ; aza $GlyNH_2$ ; or a group -NHR $_2$  where  $R_2$ is a  $(C_1-C_4)$  alkyl which may be substituted by an hydroxy or one or several fluorine atoms; a  $(C_3-C_6)$  cycloalkyl; or a heterocyclic radical selected from morpholinyl, pyrrolidinyl and piperidyl.
- 24. (previously presented): The pharmaceutical composition according to claim 23 wherein said peptide analogue has the formula (SEQ ID N° : 2):

A1-His-A3-A4-A5-A6-A7-A8-Pro-Z

(I)

- Al is pGlu, Sar or AcSar;
- A3 is an aromatic L-amino acid;
- A4 is Ala, Ser, D-Ser, MeSer, Ser(OBut), Ser(OBzl) or Thr;
- A5 is an aromatic L-amino acid;
- A6 is Gly; D-Pro; (S)-spirolactam-Pro; D-Ser; D-Thr; D-Cys ; D-Met ; D-Pen ; D-(S-Me)Pen ; D-(S-Et)Pen ; D-Ser(OBu<sup>t</sup>) ; D-Asp(OBu<sup>t</sup>); D-Glu(OBu<sup>t</sup>); D-Thr(OBu<sup>t</sup>); D-Cys(OBu<sup>t</sup>); D- $Ser(OR_1)$  where  $R_1$  is a sugar moiety; an aza-amino acid; D-His which may be substituted on the imidazole ring by a  $(C_1 C_6$ ) alkyl or a benzyl group ; an aliphatic D-amino acid with a  $(C_1-C_8)$  alkyl or a  $(C_3-C_6)$  cycloalkyl side chain; an aromatic Damino acid; D-cyclohexadienyl-Gly; D-perhydronaphtyl-Ala; Dperhydrodiphenyl-Ala ; or a basic D-amino acid ;

- A7 is a linear, branched or cyclic aliphatic L-amino acid of 3 to 20 carbon atoms which may be N-alpha-substituted by a  $(C_1-C_4)$  alkyl group optionally substituted by one or several fluorine atoms;
- A8 is a basic L-amino acid;
- Z is  $GlyNH_2$ ; aza $GlyNH_2$ ; or a group -NHR $_2$  where  $R_2$  is a ( $C_1$ - $C_4$ )alkyl which may be substituted by an hydroxy or one or several fluorine atoms; a ( $C_3$ - $C_6$ )cycloalkyl; or a heterocyclic radical selected from morpholinyl, pyrrolidinyl and piperidyl.
- 25. (previously presented): The pharmaceutical composition according to claim 24 wherein said peptide analogue has the formula (SEQ ID  $N^{\circ}$ : 3):

pGlu-His-A3-Ser-A5-A6-A7-Arg-Pro-Z  $\,$  (II) in which A7 is Leu, Tle, Nle, Hol, Npg, Cha or Ada, which may be N-alpha-substituted by a methyl or ethyl group optionally substituted by one or several fluorine atoms.

26. (previously presented): The pharmaceutical composition according to claim 24 wherein said peptide analogue has the formula (SEO ID  $N^{\circ}$ : 4):

pGlu-His-A3-Ser-A5-A6-A7-Arg-Pro-Z (III) in which:

- A3 and A5 are each independently Phe, Tyr, Trp, 2MeTrp, HPhe, HTyr, Nal, 1Nal, Bal, Pal, 4Pal, or pClPhe;
- A6 is (S)-spirolactam-Pro; Gly; D-Pro; D-Ser(OBu<sup>t</sup>); D-Asp(OBu<sup>t</sup>); D-Glu(OBu<sup>t</sup>); D-Thr(OBu<sup>t</sup>); D-Cys(OBu<sup>t</sup>); D-His or D-His(Bzl); D-Ala, D-Leu, D-Tle, D-Nle, D-Hol, D-Npg or D-Cha; D-Phe, D-HPhe, D-Tyr, D-HTyr, D-Trp, D-2MeTrp, D-Nal, D-1Nal, D-Bal, D-Pal, D-4Pal, or D-pClPhe; D-cyclohexadienyl-Gly; D-perhydronaphtyl-Ala; D-perhydrodiphenyl-Ala or D-APhe

optionally substituted by an aminotriazolyl group;

- A7 is Leu, Npg or Cha, which may be N-alpha-substituted by a methyl group;
- Z is  $GlyNH_2$ ,  $azaGlyNH_2$  or  $-NC_2H_5$ .
- 27. (previously presented): The pharmaceutical composition according to claim 24 wherein said peptide analogue has the formula (SEQ ID  $N^{\circ}$ :5):

pGlu-His-Trp-Ser-Tyr-A6-A7-Arg-Pro-Z (IV) in which:

- A6 is (S)-spirolactam-Pro, D-Leu, D-Ala, D-Nal, D-Phe, D-Ser(OBu<sup>t</sup>) or D-Trp;
- A7 is Leu, MeLeu, Npg or MeNpg;
- Z is  $GlyNH_2$ ,  $azaGlyNH_2$  or  $-NC_2H_5$ .
- 28. (previously presented): The pharmaceutical composition according to claim 24 wherein the peptide analogue is selected from the group consisting of leuprorelin,  $[Npg^7]$ -leuprorelin, triptorelin,  $[Npg^7]$ -triptorelin, goserelin,  $[Npg^7]$ -goserelin, buserelin and  $[Npg^7]$ -buserelin.
- 29. (withdrawn): The pharmaceutical composition according to claim 23 wherein said peptide analogue has the formula (SEQ ID  $N^{\circ}$ :6):

A1-A2-A3-A4-A5-A6-A7-A8-Pro-Z (I')

- Al is pGlu; D-pGlu; Sar; AcSar; Pro or a derivative thereof; Ser; D-Ser; Ac-D-Ser; Thr; D-Thr; Ac-D-Thr; or an aromatic D-amino acid which may be acylated;
- A2 is a direct bond or an aromatic D-amino acid;
- A3 is an aromatic L- or D-amino acid;

- A4 is Ala, Ser, D-Ser, MeSer, Ser(OBut), Ser(OBzl) or Thr;
- A5 is an aromatic L-amino acid or a basic L- or D-amino acid;
- A6 is Gly; D-Pro; D-Ser; D-Thr; D-Cys; D-Met; D-Asn; D-Pen; D-(S-Me)Pen; D-(S-Et)Pen; D-Ser(OBu<sup>t</sup>); D-Asp(OBu<sup>t</sup>); D-Glu(O-Bu<sup>t</sup>); D-Thr(O-Bu<sup>t</sup>); D-Cys(O-Bu<sup>t</sup>); D-Ser(O-R<sub>1</sub>) where R<sub>1</sub> is a sugar moiety; an aliphatic D-amino acid with a (C<sub>1</sub>-C<sub>8</sub>)alkyl or a (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl side chain; an aromatic D-amino acid; D-cyclohexadienyl-Gly; D-perhydronaphthyl-Ala; D-perhydrodiphenyl-Ala; or a basic L- or D-amino acid; A7 is a linear, branched or cyclic aliphatic L-amino acid of 3 to 20 carbon atoms which may be N-alpha-substituted by a

 $(C_1-C_4)$  alkyl group optionally substituted by one or several

- A8 is a basic L- or D-amino acid;
- Z is GlyNH<sub>2</sub> or D-AlaNH<sub>2</sub>.

fluorine atoms:

30. (withdrawn): The pharmaceutical composition according to claim 29 wherein the peptide analogue has the formula (SEQ ID  $N^{\circ}$ :7):

Ac-D-Nal-D-pClPhe-D-Pal-Ser-A5-A6-A7-A8-Pro-D-AlaNH<sub>2</sub> (II') in which:

- A5 is Tyr, HTyr, MeTyr, MeHTyr, NicLys or IprLys;
- A6 is (S)spirolactam-Pro, D-Arg, D-NicLys, D-IprLys, D-Cit, D-HCit or D-Asn;
- A7 is Leu, MeLeu, Npg or MeNpg;
- A8 is Arg, NicLys or IprLys.
- 31. (withdrawn): The pharmaceutical composition according to claim 29 wherein the peptide analogue is selected from the group consisting of antide,  $[Npg^7]$ -antide, cetrorelix,  $[Npg^7]$ -

cetrorelix, abarelix and  $[Npg^7]$ -abarelix.

- 32. (previously presented): The pharmaceutical composition according to claim 21 wherein the  $\alpha$ -cyclodextrin derivative is selected from the group consisting of methylated  $\alpha$ -cyclodextrin, hexakis(2,3,6-tri-O-methyl)- $\alpha$ -cyclodextrin, carboxy-methylated  $\alpha$ -cyclodextrin and phosphated  $\alpha$ -cyclodextrin.
- 33. (previously presented): The pharmaceutical composition according to claim 32 wherein the  $\alpha$ -cyclodextrin derivative is hexakis(2,3,6-tri-O-methyl)- $\alpha$ -cyclodextrin.
- 34. (currently amended): The pharmaceutical composition according to claim  $\frac{21}{23}$  which further comprises a compound selected from the group consisting of a protease inhibitor, an absorption enhancer, and mixtures thereof.
- 35. (currently amended): A method of enhancing the biological activity of a LH-RH peptide analogue which comprises orally administering to a patient in need thereof a pharmaceutical composition comprising a therapeutically effective amount of a peptide analogue in combination with  $\alpha$ -cyclodextrin and excipients suitable for the gastrointestinal delivery of the peptide analogue, wherein the  $\alpha$ -cyclodextrin enhances the biological activity of the LH-RH peptide analogue when orally administered a therapeutically effective amount of said analogue in combination with  $\alpha$ -cyclodextrin or a derivative thereof.
  - 36. (previously presented): The method according to claim

35, wherein said peptide analogue has the formula (SEQ ID  $N^{\circ}:1$ ):

A1-A2-A3-A4-A5-A6-A7-A8-Pro-Z (A)

- Al is pGlu; D-pGlu; Sar; AcSar; Pro or a derivative thereof; Ser; D-Ser; Ac-D-Ser; Thr; D-Thr; Ac-D-Thr; or an aromatic D-amino acid which may be acylated;
- A2 is a direct bond; His; or an aromatic D-amino acid;
- A3 is an aromatic L- or D-amino acid;
- A4 is Ala, Ser, D-Ser, MeSer, Ser(OBut), Ser(OBzl) or Thr;
- A5 is an aromatic L-amino acid or a basic L- or D-amino acid ;
- A6 is Gly; (S)-spirolactam-Pro; D-Pro; D-Ser; D-Thr; D-Cys; D-Met; D-Asn; D-Pen; D-(S-Me)Pen; D-(S-Et)Pen; D-Ser(OBu<sup>t</sup>); D-Asp(OBu<sup>t</sup>); D-Glu(OBu<sup>t</sup>); D-Thr(OBu<sup>t</sup>); D-Cys(OBu<sup>t</sup>); D-Ser(OR<sub>1</sub>) where R<sub>1</sub> is a sugar moiety; an aza-amino acid; D-His which may be substituted on the imidazole ring by a  $(C_1-C_6)$  alkyl, a  $(C_2-C_7)$  acyl or a benzyl group; an aliphatic D-amino acid with a  $(C_1-C_8)$  alkyl or a  $(C_3-C_6)$  cycloalkyl side chain; an aromatic D-amino acid; D-cyclohexadienyl-Gly; D-perhydronaphthyl-Ala; D-perhydrodiphenyl-Ala; or a basic L- or D-amino acid; A7 is a linear, branched or cyclic aliphatic L-amino acid of
- 3 to 20 carbon atoms which may be N-alpha-substituted by a  $(C_1-C_4)$  alkyl group optionally substituted by one or several fluorine atoms;
- A8 is a basic L- or D-amino acid;
- Z is  $GlyNH_2$ ; D-Ala $NH_2$ ; aza $GlyNH_2$ ; or a group -NHR $_2$  where  $R_2$  is a  $(C_1-C_4)$  alkyl which may be substituted by an hydroxy or one or several fluorine atoms; a  $(C_3-C_6)$  cycloalkyl; or a heterocyclic radical selected from morpholinyl, pyrrolidinyl and piperidyl.

37. (previously presented): The method according to claim 36 wherein said peptide analogue has the formula (SEQ ID N $^{\circ}$ : 2):

A1-His-A3-A4-A5-A6-A7-A8-Pro-Z (I)

- Al is pGlu, Sar or AcSar;
- A3 is an aromatic L-amino acid;
- A4 is Ala, Ser, D-Ser, MeSer, Ser(OBut), Ser(OBzl) or Thr;
- A5 is an aromatic L-amino acid;
- A6 is Gly; D-Pro; (S)-spirolactam-Pro; D-Ser; D-Thr; D-Cys; D-Met; D-Pen; D-(S-Me)Pen; D-(S-Et)Pen; D-Ser(OBu<sup>t</sup>); D-Asp(OBu<sup>t</sup>); D-Glu(OBu<sup>t</sup>); D-Thr(OBu<sup>t</sup>); D-Cys(OBu<sup>t</sup>); D-Ser(OR<sub>1</sub>) where R<sub>1</sub> is a sugar moiety; an aza-amino acid; D-His which may be substituted on the imidazole ring by a (C<sub>1</sub>-C<sub>6</sub>)alkyl or a benzyl group; an aliphatic D-amino acid with a (C<sub>1</sub>-C<sub>6</sub>)alkyl or a (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl side chain; an aromatic D-amino acid; D-cyclohexadienyl-Gly; D-perhydronaphtyl-Ala; D-perhydrodiphenyl-Ala; or a basic D-amino acid;
- A7 is a linear, branched or cyclic aliphatic L-amino acid of 3 to 20 carbon atoms which may be N-alpha-substituted by a  $(C_1-C_4)$  alkyl group optionally substituted by one or several fluorine atoms;
- A8 is a basic L-amino acid;
- Z is  $GlyNH_2$ ; aza $GlyNH_2$ ; or a group -NHR<sub>2</sub> where R<sub>2</sub> is a (C<sub>1</sub>-C<sub>4</sub>)alkyl which may be substituted by an hydroxy or one or several fluorine atoms; a (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl; or a heterocyclic radical selected from morpholinyl, pyrrolidinyl and piperidyl.
- 38. (previously presented): The method according to claim 37 wherein said peptide analogue has the formula (SEQ ID  $N^{\circ}$ :

3):

pGlu-His-A3-Ser-A5-A6-A7-Arg-Pro-Z (II) in which A7 is Leu, Tle, Nle, Hol, Npg, Cha or Ada, which may be N-alpha-substituted by a methyl or ethyl group optionally substituted by one or several fluorine atoms.

39. (previously presented): The method according to claim 37 wherein said peptide analogue has the formula (SEQ ID  $N^{\circ}$ :

pGlu-His-A3-Ser-A5-A6-A7-Arg-Pro-Z (III) in which:

- A3 and A5 are each independently Phe, Tyr, Trp, 2MeTrp, HPhe, HTyr, Nal, 1Nal, Bal, Pal, 4Pal, or pClPhe;
   A6 is (S)-spirolactam-Pro; Gly; D-Pro; D-Ser(OBu<sup>t</sup>); D-Asp(OBu<sup>t</sup>); D-Glu(OBu<sup>t</sup>); D-Thr(OBu<sup>t</sup>); D-Cys(OBu<sup>t</sup>); D-His or D-His(Bzl); D-Ala, D-Leu, D-Tle, D-Nle, D-Hol, D-Npg or D-Cha; D-Phe, D-HPhe, D-Tyr, D-HTyr, D-Trp, D-2MeTrp, D-Nal, D-1Nal, D-Bal, D-Pal, D-4Pal, or D-pClPhe; D-cyclohexadienyl-Gly; D-perhydronaphtyl-Ala; D-perhydrodiphenyl-Ala; or D-APhe optionally substituted by an aminotriazolyl group;
   A7 is Leu, Npg or Cha, which may be N-alpha-substituted by a methyl group;
- Z is  $GlyNH_2$ ;  $azaGlyNH_2$  or  $-NC_2H_5$ .
- 40. (previously presented): The method according to claim 37 wherein said peptide analogue has the formula (SEQ ID  $N^{\circ}$ : 5):

pGlu-His-Trp-Ser-Tyr-A6-A7-Arg-Pro-Z (IV) in which:

- A6 is (S)-spirolactam-Pro, D-Leu, D-Ala, D-Nal, D-Phe, D-Ser(OBu<sup>t</sup>) or D-Trp;
- A7 is Leu, MeLeu, Npg or MeNpg;

- Z is  $GlyNH_2$ ;  $azaGlyNH_2$  or  $-NC_2H_5$ .
- 41. (previously presented): The method according to claim 37 wherein the peptide analogue is selected from the group consisting of leuprorelin,  $[Npg^7]$ -leuprorelin, triptorelin,  $[Npg^7]$ -triptorelin, goserelin,  $[Npg^7]$ -goserelin, buserelin and  $[Npg^7]$ -buserelin.
- 42. (withdrawn): The method according to claim 36 wherein said peptide analogue has the formula (SEQ ID  $N^{\circ}$ : 6):

A1-A2-A3-A4-A5-A6-A7-A8-Pro-Z (I')

- Al is pGlu; D-pGlu; Sar; AcSar; Pro or a derivative thereof; Ser; D-Ser; Ac-D-Ser; Thr; D-Thr; Ac-D-Thr; or an aromatic D-amino acid which may be acylated;
- A2 is a direct bond or an aromatic D-amino acid;
- A3 is an aromatic L- or D-amino acid;
- A4 is Ala, Ser, D-Ser, MeSer, Ser(OBu<sup>t</sup>), Ser(OBzl) or Thr;
- A5 is an aromatic L-amino acid or a basic L- or D-amino acid;
- A6 is Gly; D-Pro; D-Ser; D-Thr; D-Cys; D-Met; D-Asn; D-Pen; D-(S-Me)Pen; D-(S-Et)Pen; D-Ser(OBu<sup>t</sup>); D-Asp(OBu<sup>t</sup>); D-Glu(O-Bu<sup>t</sup>); D-Thr(O-Bu<sup>t</sup>); D-Cys(O-Bu<sup>t</sup>); D-Ser(O-R<sub>1</sub>) where R<sub>1</sub> is a sugar moiety; an aliphatic D-amino acid with a (C<sub>1</sub>-C<sub>8</sub>)alkyl or a (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl side chain; an aromatic D-amino acid; D-cyclohexadienyl-Gly; D-perhydronaphthyl-Ala; D-perhydrodiphenyl-Ala; or a basic L- or D-amino acid; A7 is a linear, branched or cyclic aliphatic L-amino acid of 3 to 20 carbon atoms which may be N-alpha-substituted by a (C<sub>1</sub>-C<sub>4</sub>)alkyl group optionally substituted by one or several fluorine atoms;

- A8 is a basic L- or D-amino acid;
- Z is GlyNH<sub>2</sub> or D-AlaNH<sub>2</sub>.
- 43. (withdrawn): The method according to claim 42 wherein the peptide analogue has the formula (SEQ ID N $^{\circ}$ : 7): Ac-D-Nal-D-pClPhe-D-Pal-Ser-A5-A6-A7-A8-Pro-D-AlaNH $_2$  (II') in which:
- A5 is Tyr, HTyr, MeTyr, MeHTyr, NicLys or IprLys;
- A6 is (S)spirolactam-Pro, D-Arg, D-NicLys, D-IprLys, D-Cit, D-HCit or D-Asn;
- A7 is Leu, MeLeu, Npg or MeNpg;
- A8 is Arg, NicLys or IprLys.
- 44. (withdrawn): The method according to claim 42 wherein the peptide analogue is selected from the group consisting of antide,  $[Npg^7]$ -antide, cetrorelix,  $[Npg^7]$ -cetrorelix, abarelix and  $[Npg^7]$ -abarelix.
- 45. (previously presented): The method according to claim 35 wherein the  $\alpha$ -cyclodextrin derivative is selected from the group consisting of methylated  $\alpha$ -cyclodextrin, hexakis(2,3,6-tri-O-methyl)- $\alpha$ -cyclodextrin, carboxymethylated  $\alpha$ -cyclodextrin and phosphated  $\alpha$ -cyclodextrin.
- 46. (previously presented): The method according to claim 45 wherein the  $\alpha$ -cyclodextrin derivative is hexakis(2,3,6-tri-0-methyl)- $\alpha$ -cyclodextrin.
- 47. (previously presented): A method of treating a disease wherein a LH-RH agonist or antagonist action is required which comprises orally administering to a patient in need thereof a

therapeutically effective amount of a LH-RH peptide analogue in combination with  $\alpha\text{-cyclodextrin}$  or a derivative thereof, wherein said peptide analogue has the formula (SEQ ID N°: 1)

## A1-A2-A3-A4-A5-A6-A7-A8-Pro-Z (A)

- Al is pGlu; D-pGlu; Sar; AcSar; Pro or a derivative thereof; Ser; D-Ser; Ac-D-Ser; Thr; D-Thr; Ac-D-Thr; or an aromatic D-amino acid which may be acylated;
- A2 is a direct bond; His; or an aromatic D-amino acid;
- A3 is an aromatic L- or D-amino acid;
- A4 is Ala, Ser, D-Ser, MeSer, Ser(OBut), Ser(OBzl) or Thr;
- A5 is an aromatic L-amino acid or a basic L- or D-amino acid :
- A6 is Gly; (S)-spirolactam-Pro; D-Pro; D-Ser; D-Thr; D-Cys; D-Met; D-Asn; D-Pen; D-(S-Me)Pen; D-(S-Et)Pen; D-Ser(OBu<sup>t</sup>); D-Asp(OBu<sup>t</sup>); D-Glu(OBu<sup>t</sup>); D-Thr(OBu<sup>t</sup>); D-Cys(OBu<sup>t</sup>); D-Ser(OR<sub>1</sub>) where R<sub>1</sub> is a sugar moiety; an aza-amino acid; D-His which may be substituted on the imidazole ring by a (C<sub>1</sub>-C<sub>6</sub>)alkyl, a (C<sub>2</sub>-C<sub>7</sub>)acyl or a benzyl group; an aliphatic D-amino acid with a (C<sub>1</sub>-C<sub>8</sub>)alkyl or a (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl side chain; an aromatic D-amino acid; D-cyclohexadienyl-Gly; D-perhydronaphthyl-Ala; D-perhydrodiphenyl-Ala; or a basic L- or D-amino acid;
- A7 is a linear, branched or cyclic aliphatic L-amino acid of 3 to 20 carbon atoms which may be N-alpha-substituted by a  $(C_1-C_4)$  alkyl group optionally substituted by one or several fluorine atoms;
- A8 is a basic L- or D-amino acid;
- Z is  $GlyNH_2$ ; D-Ala $NH_2$ ; aza $GlyNH_2$ ; or a group -NHR $_2$  where  $R_2$  is a  $(C_1-C_4)$  alkyl which may be substituted by an hydroxy or one or several fluorine atoms; a  $(C_3-C_6)$  cycloalkyl; or a

heterocyclic radical selected from morpholinyl, pyrrolidinyl and piperidyl.

48. (previously presented): The method according to claim 47 wherein said peptide analogue has the formula (SEQ ID  $N^{\circ}$ : 2):

A1-His-A3-A4-A5-A6-A7-A8-Pro-Z (I)

- Al is pGlu, Sar or AcSar;
- A3 is an aromatic L-amino acid;
- A4 is Ala, Ser, D-Ser, MeSer, Ser(OBut), Ser(OBzl) or Thr;
- A5 is an aromatic L-amino acid;
- A6 is Gly; D-Pro; (S)-spirolactam-Pro; D-Ser; D-Thr; D-Cys; D-Met; D-Pen; D-(S-Me)Pen; D-(S-Et)Pen; D-Ser(OBu<sup>t</sup>); D-Asp(OBu<sup>t</sup>); D-Glu(OBu<sup>t</sup>); D-Thr(OBu<sup>t</sup>); D-Cys(OBu<sup>t</sup>); D-Ser(OR<sub>1</sub>) where R<sub>1</sub> is a sugar moiety; an aza-amino acid; D-His which may be substituted on the imidazole ring by a (C<sub>1</sub>-C<sub>6</sub>)alkyl or a benzyl group; an aliphatic D-amino acid with a (C<sub>1</sub>-C<sub>8</sub>)alkyl or a (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl side chain; an aromatic D-amino acid; D-cyclohexadienyl-Gly; D-perhydronaphtyl-Ala; D-perhydrodiphenyl-Ala; or a basic D-amino acid;
- A7 is a linear, branched or cyclic aliphatic L-amino acid of 3 to 20 carbon atoms which may be N-alpha-substituted by a  $(C_1-C_4)$  alkyl group optionally substituted by one or several fluorine atoms;
- A8 is a basic L-amino acid;
- Z is  $GlyNH_2$ ; aza $GlyNH_2$ ; or a group -NHR<sub>2</sub> where R<sub>2</sub> is a (C<sub>1</sub>-C<sub>4</sub>)alkyl which may be substituted by an hydroxy or one or several fluorine atoms; a (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl; or a heterocyclic radical selected from morpholinyl, pyrrolidinyl and piperidyl.

49. (previously presented): The method according to claim 48 wherein said peptide analogue has the formula (SEQ ID  $N^{\circ}:3$ ):

pGlu-His-A3-Ser-A5-A6-A7-Arg-Pro-Z (II) in which A7 is Leu, Tle, Nle, Hol, Npg, Cha or Ada, which may be N-alpha-substituted by a methyl or ethyl group optionally substituted by one or several fluorine atoms.

50. (previously presented): The method according to claim 48 wherein said peptide analogue has the formula (SEQ ID  $N^{\circ}$ : 4):

pGlu-His-A3-Ser-A5-A6-A7-Arg-Pro-Z (III) in which:

- A3 and A5 are each independently Phe, Tyr, Trp, 2MeTrp,
  HPhe, HTyr, Nal, 1Nal, Bal, Pal, 4Pal, or pClPhe;
   A6 is (S)-spirolactam-Pro; Gly; D-Pro; D-Ser(OBu<sup>t</sup>); DAsp(OBu<sup>t</sup>); D-Glu(OBu<sup>t</sup>); D-Thr(OBu<sup>t</sup>); D-Cys(OBu<sup>t</sup>); D-His or
  D-His(Bzl); D-Ala, D-Leu, D-Tle, D-Nle, D-Hol, D-Npg or D-Cha; D-Phe, D-HPhe, D-Tyr, D-HTyr, D-Trp, D-2MeTrp, D-Nal, D1Nal, D-Bal, D-Pal, D-4Pal, or D-pClPhe; D-cyclohexadienyl-Gly; D-perhydronaphtyl-Ala; D-perhydrodiphenyl-Ala; or D-APhe
  optionally substituted by an aminotriazolyl group;
   A7 is Leu, Npg or Cha, which may be N-alpha-substituted by a
  methyl group;
- Z is  $GlyNH_2$ ;  $azaGlyNH_2$  or  $-NC_2H_5$ .
- 51. (previously presented): The method according to claim 48 wherein said peptide analogue has the formula (SEQ ID  $N^{\circ}$ : 5):

pGlu-His-Trp-Ser-Tyr-A6-A7-Arg-Pro-Z (IV) in which:

- A6 is (S)-spirolactam-Pro, D-Leu, D-Ala, D-Nal, D-Phe, D-

Ser(OBut) or D-Trp;

- A7 is Leu, MeLeu, Npg or MeNpg;
- Z is  $GlyNH_2$ ;  $azaGlyNH_2$  or  $-NC_2H_5$ .
- 52. (previously presented): The method according to claim 48 wherein the peptide analogue is selected from the group consisting of leuprorelin, [Npg<sup>7</sup>]-leuprorelin, triptorelin,  $[Npg^7]$ -triptorelin, goserelin,  $[Npg^7]$ -goserelin, buserelin and [Npq<sup>7</sup>]-buserelin.
- 53. (withdrawn): The method according to claim 47 wherein said peptide analogue has the formula (SEQ ID N°: 6):

A1-A2-A3-A4-A5-A6-A7-A8-Pro-Z (I')

- Al is pGlu; D-pGlu; Sar; AcSar; Pro or a derivative thereof; Ser; D-Ser; Ac-D-Ser; Thr; D-Thr; Ac-D-Thr; or an aromatic D-amino acid which may be acylated;
- A2 is a direct bond or an aromatic D-amino acid;
- A3 is an aromatic L- or D-amino acid;
- A4 is Ala, Ser, D-Ser, MeSer, Ser(OBut), Ser(OBzl) or Thr;
- A5 is an aromatic L-amino acid or a basic L- or D-amino acid;
- A6 is Gly; D-Pro; D-Ser; D-Thr; D-Cys; D-Met; D-Asn; D-Pen; D-(S-Me)Pen; D-(S-Et)Pen; D-Ser(OBut); D-Asp(OBut);  $D-Glu(O-Bu^t)$ ;  $D-Thr(O-Bu^t)$ ;  $D-Cys(O-Bu^t)$ ;  $D-Ser(O-R_1)$  where  $R_1$  is a sugar moiety; an aliphatic D-amino acid with a  $(C_1$ - $C_8$ ) alkyl or a  $(C_3-C_6)$  cycloalkyl side chain; an aromatic Damino acid; D-cyclohexadienyl-Gly; D-perhydronaphthyl-Ala; D-perhydrodiphenyl-Ala; or a basic L- or D-amino acid; - A7 is a linear, branched or cyclic aliphatic L-amino acid of
- 3 to 20 carbon atoms which may be N-alpha-substituted by a

 $(C_1-C_4)$  alkyl group optionally substituted by one or several fluorine atoms;

- A8 is a basic L- or D-amino acid;
- Z is GlyNH<sub>2</sub> or D-AlaNH<sub>2</sub>.
- 54. (withdrawn): The method according to claim 53 wherein the peptide analogue has the formula (SEQ ID N $^{\circ}$ : 7): Ac-D-Nal-D-pClPhe-D-Pal-Ser-A5-A6-A7-A8-Pro-D-AlaNH $_2$  (II') in which:
- A5 is Tyr, HTyr, MeTyr, MeHTyr, NicLys or IprLys;
- A6 is (S)spirolactam-Pro, D-Arg, D-NicLys, D-IprLys, D-Cit, D-HCit or D-Asn;
- A7 is Leu, MeLeu, Npg or MeNpg;
- A8 is Arg, NicLys or IprLys.
- 55. (withdrawn): The method according to claim 53 wherein the peptide analogue is selected from the group consisting of antide,  $[Npg^7]$ -antide, cetrorelix,  $[Npg^7]$ -cetrorelix, abarelix and  $[Npg^7]$ -abarelix.
- 56. (withdrawn): The method according to claim 47 wherein the  $\alpha$ -cyclodextrin derivative is selected from the group consisting of methylated  $\alpha$ -cyclodextrin, hexakis(2,3,6-tri-0-methyl)- $\alpha$ -cyclodextrin, carboxymethylated  $\alpha$ -cyclodextrin and phosphated  $\alpha$ -cyclodextrin.
- 57. (withdrawn): The method according to claim 56 wherein the  $\alpha$ -cyclodextrin derivative is hexakis(2,3,6-tri-0-methyl)-  $\alpha$ -cyclodextrin.
  - 58. (previously presented): The method according to claim

- 47 for the treatment or prevention of breast cancer.
- 59. (previously presented): The method according to claim 58 which further comprises the sequential, parallel or over a period of time administration of at least one compound selected from the group consisting of an antiestrogen, an aromatase inhibitor and a  $C_{17-20}$  lyase inhibitor.
- 60. (previously presented): The method according to claim 47 for the treatment or prevention of prostate cancer or benign prostatic hypertrophy.
- 61. (previously presented): The method according to claim 60 which further comprises the sequential, parallel or over a period of time administration of at least one compound selected from the group consisting of an antiandrogen, a  $5\alpha$ -reductase inhibitor and a  $C_{17-20}$  lyase inhibitor.
- 62. (previously presented): The method according to claim 47 wherein the peptide analogue is delivered to the gastrointestinal tract of the patient.
- 63. (previously presented): The pharmaceutical composition according to claim 28 wherein the  $\alpha$ -cyclodextrin derivative is selected from the group consisting of methylated  $\alpha$ -cyclodextrin, hexakis(2,3,6-tri-O-methyl)- $\alpha$ -cyclodextrin, carboxy-methylated  $\alpha$ -cyclodextrin and phosphated  $\alpha$ -cyclodextrin.
- 64. (previously presented): The pharmaceutical composition according to claim 28 comprising  $\alpha\text{-cyclodextrin}$  or

hexakis(2,3,6-tri-0-methyl)- $\alpha$ -cyclodextrin.

- 65. (previously presented): The pharmaceutical composition according to claim 64 wherein the peptide analogue is leuprorelin.
- 66. (previously presented): The pharmaceutical composition according to claim 64 wherein the peptide analogue is  $[Npg^7]$ -leuprorelin.
- 67. (previously presented): The method according to claim 41 wherein the  $\alpha$ -cyclodextrin derivative is selected from the group consisting of methylated  $\alpha$ -cyclodextrin, hexakis(2,3,6-tri-O-methyl)- $\alpha$ -cyclodextrin, carboxymethylated  $\alpha$ -cyclodextrin and phosphated  $\alpha$ -cyclodextrin.
- 68. (previously presented): The method according to claim 67 wherein the  $\alpha$ -cyclodextrin derivative is hexakis(2,3,6-tri-O-methyl)- $\alpha$ -cyclodextrin.
- 69. (previously presented): The method according to claim 35, which comprises orally administering a therapeutically effective amount of leuprorelin in combination with  $\alpha$ -cyclodextrin or hexakis(2,3,6-tri-O-methyl)- $\alpha$ -cyclodextrin.
- 70. (previously presented): The method according to claim 35, which comprises orally administering a therapeutically effective amount of [Npg<sup>7</sup>]-leuprorelin in combination with  $\alpha$ -cyclodextrin or hexakis(2,3,6-tri-O-methyl)- $\alpha$ -cyclodextrin.

- 71. (previously presented): The method according to claim 52 wherein the  $\alpha$ -cyclodextrin derivative is selected from the group consisting of methylated  $\alpha$ -cyclodextrin, hexakis(2,3,6-tri-O-methyl)- $\alpha$ -cyclodextrin, carboxymethylated  $\alpha$ -cyclodextrin and phosphated  $\alpha$ -cyclodextrin.
- 72. (previously presented): The method according to claim 71 wherein the  $\alpha$ -cyclodextrin derivative is hexakis(2,3,6-tri-0-methyl)- $\alpha$ -cyclodextrin.
- 73. (previously presented): The method according to claim 47, which comprises orally administering a therapeutically effective amount of leuprorelin in combination with  $\alpha$ -cyclodextrin or hexakis(2,3,6-tri-O-methyl)- $\alpha$ -cyclodextrin.
- 74. (previously presented): The method according to claim 47, which comprises orally administering a therapeutically effective amount of  $[Npg^7]$ -leuprorelin in combination with  $\alpha$ -cyclodextrin or hexakis(2,3,6-tri-O-methyl)- $\alpha$ -cyclodextrin.
- 75. (previously presented): The method according to claim 62 wherein the  $\alpha$ -cyclodextrin derivative is selected from the group consisting of methylated  $\alpha$ -cyclodextrin, hexakis(2,3,6-tri-O-methyl)- $\alpha$ -cyclodextrin, carboxymethylated  $\alpha$ -cyclodextrin and phosphated  $\alpha$ -cyclodextrin.
- 76. (previously presented): The method according to claim 71 wherein the  $\alpha$ -cyclodextrin derivative is hexakis(2,3,6-tri-O-methyl)- $\alpha$ -cyclodextrin.

- 77. (previously presented): The method according to claim 76 wherein the peptide analogue is leuprorelin.
- 78. (previously presented): The method according to claim 76 wherein the peptide analogue is  $[Npg^7]$ -leuprorelin.